Exhibit B

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
CHARLESTON DIVISION

IN RE: ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION	**Master File No. 2:12-MD-02327 MDL 2327** **JOSEPH R. GOODWIN U.S. DISTRICT JUDGE**
THIS DOCUMENT RELATES TO WAVE 2 CASES	

EXPERT REPORT OF TIMOTHY MCKINNEY, MD ON TVT

This report contains a summary of my qualifications, education, training, and experience, a statement of my opinions that I have formed to date, the bases for those opinions, and the information I considered in forming my opinions. All of my opinions are based on my education, training, clinical experience, the pertinent medical literature, discussions with colleagues, and other materials I have reviewed. Materials that support my findings and opinions, including documents that I have reviewed, are identified either in this report or are listed in the attached reliance materials list.

All of the opinions I express in this report are held to a reasonable degree of medical and scientific probability and certainty. If I receive additional information after signing this report but before trial, I may form additional or different opinions.

I. Background

a. Education, Training, and Experience

I attended Bucknell University, graduating with a Bachelor of Science degree in biochemistry.

I graduated from Rutgers Medical School in New Jersey in 1987. I did my internship and residency in OB/Gyn at Cooper Hospital University Medical Center in Camden, NJ from 1987 to 1991. I then did a fellowship in urogynecology at Pennsylvania Hospital (part of U of Pennsylvania) in Philadelphia.

I became a Diplomate of the American Board of OB/ GYN in 1994_and am subspecialty board certified in Female Pelvic Medicine and Reconstructive Surgery (FPMRS) in August 2013. I am an active member of the American Urological Association (AUA), the American Urogynecology Society(AUGS), Society of Urodynamic and Female Urology (SUFU), International Urogynecology Association (IUGA), European Association of Urology (EAU), International Continence Society (ICS), ISGL, and American Association of Gynecological Laparoscopy (AAGL). I am a Professor at Drexel University College of Medicine in Philadelphia, Pennsylvania and part of the fellowship training program for MIS and FPMRS. I taught 100's of courses on pelvic reconstruction and incontinence repair by all techniques including, vaginal, laparoscopic and open. Incontinence, pelvic/ vaginal/ bladder pain evaluation, diagnosis, and treatment where also part of the courses. I published an abstracts as early as 1994 about a comparative study of laparoscopic retropubic urethropexy with Prolene mesh and classic Burch suspension, addressing 56 cases in which we had one-year follow up. I authored several chapters about pelvic floor surgery and incontinence surgery one which was published in May of 2007 . We discussed the theory that isolated breaks in the endopelvic fascia as described by Cullen Richardson, MD were the key to pelvic floor support and needed to be addressed during reparative pelvic surgery. I was a co- author on the first North American experience/ data on TVT with results

of 95 cases published in 1999. I worked with Dr. Ulmsten the inventor of TVT and through our discussions invented the TDOC "Air-changed " urodynamic catheters used in 83% of the diagnosis of voiding dysfunction and incontinence in USA and worldwide.

In addition to my public literature, In January, 2013 my partner and I were chosen as one of the few sites to participate by AMS in their post-marketing studies on Elevate (522). We were chosen to do all 3 arms of the study, anterior elevate, posterior elevate and native tissue repairs for our skills and qualifications.

I at one time had a consulting role with Ethicon regarding pelvic surgery and incontinence procedures such as laparoscopic burch and TVT. For example, I was a contributor to the resource monograph. I was invited to panel discussions. I was a preceptor.

I was also a consultant to AMS in an important period of time after the 2011 FDA warning.

It is clear that pelvic surgeons adopted mesh into the pelvic space from the success of hernia surgeons. Gynecologic surgeons were using hernia mesh long before products like Gynemesh PS were launched. I not only used them for POP, but for mid-urethral sling procedures as well.

I cut and shaped the Gynemesh PS for a modified burch procedure for incontinence. Burch use was replaced by the TVT and I was one of the 1st to learn Dr. Ulmsten's technique and practiced and studied TVT on cadavers due to my access to use cadavers in courses and then IMET a company I helped start to teach anatomy. It's also where I gained extensive experience with the augmentations using graft materials before applying that knowledge to the patients. I consider myself one of the world's foremost experts in pelvic anatomy.

b. Clinical Experience & Personal Experience with Stress Urinary Incontinence and Pelvic Organ Prolapse Treatments

I have a special focus in female pelvic medicine and surgery. Over the course of my career, I have performed various types of native tissue surgery and have a large study of use of the uterosacral ligaments for support and worked with Cullen Richardson on pioneering site specific repairs. I helped start a company to teach anatomy on unembalmed cadavers to do a more anatomical repair then what was in the past. The frustration to all of us is that native tissue, which in this population of patients is inherently poor, had an unacceptable failure rate. Thus, as with the surgeons' frustration over failures in hernias they started using and augmenting their repairs with mesh material. In 1995 was the 1st prospective randomized trial looking at incontinence procedures, Bergman's.[1] He found the standard procedure of Kelly Plication to have a 37% 5 year success rate. The Stamey needle suspension had a miserable 42 % success. The Burch abdominal incision procedure had an 82% success.

Native tissue prolapse repairs have high rates of recurrence. The use worldwide of a minimally invasive surgery, TVT for stress incontinence was launched in 1994 and brought to the USA in 1996 has a high rate of success 83-94% with less risks. I used surgery utilizing mesh, such as Ethicon's TVT and TVT-O mid-urethral slings, AMS, miniarc, retroarc, , Vesica In situ sling, Stamey cystourethropexy, Remex adjustable slings and Burch procedures

Please find as Exhibit A my CV

[1] Bergman A, Elia G. Three surgical procedures for genuine stress incontinence: five-year follow-up of a prospective randomized study. Am J Obstet Gynecol. 1995;173:66–71.

c. Litigation Consulting Work

During the previous four years, I have testified as an expert witness at trial or by deposition in less than a handful of cases.

I am being compensated $675.00 per hour for my study and work in this case and $6000.00 plus expenses for depositions and court.

III. Background

Urinary incontinence, including stress and urge incontinence, are common conditions in women. There are many risk factors for incontinence, and more specifically stress urinary incontinence.

Incontinence can be very distressing and burdensome to women and can cause adverse effects on women physically, mentally, and socially. Incontinence can adversely affect quality of life and relationships.

Stress urinary incontinence can be treated with lifestyle changes and behavioral therapy, non-surgical options and surgery. More conservative efforts to treat incontinence may not be a suitable option for some women and they may not always provide relief. Many women who try more conservative measures will discontinue the therapy.

Surgery for stress urinary incontinence has been shown to be the most definitive treatment. Surgeries include the Burch colposuspension, native/biologic tissue slings and most often, synthetic slings made of monofilament, large

pore polypropylene like that used in TVT and TVT-O. The clinical data shows that the TVT and TVT-O Type 1 macroporous Prolene polypropylene mesh is biocompatible, has a minimal inflammatory response, allows for adequate tissue ingrowth and is not associated with a significantly increased risk of infection over that generally associated with SUI and vaginal surgery, which is consistent with my clinical experience in hundreds of women. The data in women does not support that the TVT and TVT-O mesh is cytotoxic, causes an adverse inflammatory response, sarcoma or cancer, or that the way the edges are cut has any clinically significant effect. The data in women also does not support that the TVT and TVT-O mesh degrades, or that if it did it would have a clinically significant effect, and I have not seen evidence of mesh degradation in my clinical practice.

The TVT and TVT-O have a positive benefit to risk profile. Overall, the TVT and TVT-O have a better benefit/risk profile than the Burch and native tissue slings. The TVT and TVT-O have great utility to surgeons and their patients. Extensive data exist which supports the TVT and TVT-O and shows that they are minimally invasive and less invasive than the Burch and native tissue slings. Advantages include shorter operative time/anesthetic need, reduced surgical pain, reduced hospitalization, faster recovery, and reduced complications, including voiding dysfunction. Polypropylene mesh has been used for decades. TVT and TVT-O are safe and effective surgical options for the treatment of SUI.

The TVT and TVT-O slings have been extensively studied. The TVT and TVT-O slings have been studied in over 100 Randomized Controlled Trials (RCTs) and hundreds of other studies. The TVT and TVT-O have also been extensively

used in clinical practice by urologists, gynecologists, and urogynecologists. The TVT and TVT-O are taught to doctors during residency and fellowship because they are recognized as a suitable surgical options to treat stress urinary incontinence.

The TVT and the TVT-O are the Gold Standard and standard of care for treating stress urinary incontinence. Overall cure and improvement rates are generally in the 80-95% range with significant improvements in symptoms and quality of life. Complications are infrequent and manageable. The rate of mesh exposure is 1-2%, voiding dysfunction and retention is about 1-4%, and complications requiring surgical management occur at a rate of 2-4%. Dyspareunia and pain are also rare (<1%) and occur more often with the Burch and native tissue slings. Thus the risk of surgery due to mesh exposure or erosion, voiding dysfunction and retention, and pain is rare even out to 10-17 years follow up according to high level data. The need for a second revision is very uncommon according to the reliable scientific data. Case reports and case series are of limited value and do not address the incidence of complications or primary and secondary management.

 The TVT and TVT-O have been studied and evaluated by members of the pertinent medical and surgical organizations, such as the American Urologic Association (AUA), Society of Urodynamics, Female Pelvic Medicine and Urogenital Reconstruction (SUFU), American Urogynecologic Society (AUGS), International Continence Society (ICS), National Institute for Health and Care Excellence (NICE), Society of Gynecologic Surgeons (SGS), International Urogynecological Association (IUGA), and the European

Association of Urology (EAU), and are found to be safe and effective and widely recognized as the Gold Standard, standard of care, and first line and suitable surgical option to treat stress urinary incontinence.

All surgeries to treat stress urinary incontinence have risks. Like the TVT and TVT-O, other SUI surgeries are performed in the pelvis and utilize surgical instruments, like Stamey needles, in the surgical field. Potential risks of operating in this area are well described to surgeons during training, in medical textbooks, and in the medical literature, and are well known risks. The same is true for the tensioning of sutures as well as slings, whether made of synthetic or animal or native tissue, and the potential complications such as voiding dysfunction. Pain, pelvic pain, and dyspareunia can occur with any SUI surgery and vaginal surgery, are well known and described in the literature, as well as taught to surgeons in their education and training. Dyspareunia and sexual dysfunction that preexists in women can also be cured or improve following TVT or TVT-O placement. Mesh exposure/erosion is the only unique risk when using the TVT and TVT-O and it is uncommon and can be easily treated in the majority of cases. Suture and sling erosion and wound complications can occur with non-TVT/TVT-O SUI surgeries. The TVT and TVT-O are not defective in their design and from my perspective as a surgeon, the risks are adequately described in the IFU and professional education materials.

 Although some of Plaintiffs' experts claims that another material, such as PVDF, Prolene Soft, Vypro or Ultrapro that has been used in hernia and prolapse repair, should be used, they point to no similar breadth and length of clinical data in SUI patients to make such comparisons.

Nor have they provided data showing that these meshes would work long term in the design of the TVT or TVT-O, which have long term data. These meshes have not been studied to treat SUI in women like TVT and TVT-O. These claims are without adequate scientific support and merit.

III. MATERIALS REVIEWED

I have reviewed the IFU for Ethicon's TVT-O product, the Patient Brochure, as well as the professional education materials used by Ethicon relating to the TVT and TVT-O procedures. Through my training, clinical and surgical experience, professional activities including CME and conference attendance, my lecturing and professional education to other pelvic floor surgeons, and my review of the literature, I am familiar with urinary incontinence, the treatment of incontinence, the TVT and TVT-O, and the medical literature relating to the development of TVT and TVT-O and their safety and effectiveness. In preparation for my testimony, I have reviewed some of that literature, as set out in **Exhibit "B**." (TVT Medical Literature, SUI Mesh Documents Binder 1 and 2) Exhibits that will be used to support my findings and opinions, as well as documents that I have reviewed, are identified above, cited in my report, and listed in **Exhibit "B**" as well. These materials , in addition to my personal experience, knowledge, training, and education, have formed my opinions which follow.

Surgical Treatment of SUI -- TVT / TVT-O

Surgery for SUI has been shown to be the most definitive treatment. Surgery for SUI includes the Burch colposuspension, native/biologic tissue slings and most often, synthetic slings. Monofilament, large pore polypropylene like that used in TVT and TVT- O, is the most common type of synthetic material used in slings.

The TVT and TVT-O slings have been studied extensively, in over 100 randomized controlled trials (RCTs) and many more other studies, systematic reviews, Cochrane Reviews, metaanalyses, professional society guidelines, analyses, reviews, and position statements. These data are of the highest level of medical and scientific evidence pursuant to the Oxford Levels of Evidence as shown below in the levels of evidence pyramid:

(http://www.cebi.ox.ac.uk/for-practitioners/what-is-good-evidence.html)

My opinions are based on these high level data and thus my opinions are evidence based, unlike to Plaintiffs' experts who rely on materials which are of the lowest level evidence such as case reports and case series, and in many cases simply irrelevant such as emails, documents, literature and excerpts of testimony concerning hernia mesh and prolapse devices.

The data on the TVT and TVT-O surpasses that of other procedures like the Burch colposuspension and the autologous pubovaginal sling, as well as all other slings. Of all the sling procedures, the Type 1 macroporous, monofilament, polypropylene mesh used in the TVT and TVT-O has the longest and broadest track record of safe and effective use. Other types of surgeries to treat SUI in the past, such as Marshall- Marchetti-Krantz (MMK) procedure, anterior colporrhaphy and needle suspension procedures, have declined and are not now recommended by the pertinent medical associations.

The Burch colposuspension procedure can be performed open or laparoscopically under general anesthesia. Access to the bladder and urethra is achieved by making an incision in the abdominal wall. In the Burch, the vaginal wall is attached to the Cooper's ligament next to the pubic bone. Cystoscopy may also be performed during the Burch. Patients are required to stay in the hospital longer than for a TVT procedure, which can be performed

with local or regional anesthetic. Surgery and recovery times are longer with the Burch compared to the TVT. Although the laparoscopic approach to the Burch is available to some physicians, disadvantages include the difficulty in teaching the technique, a steep learning curve for laparoscopic suturing, the requirement for general anesthesia, abdominal entry, pneumoperitoneum, and three or four abdominal incisions. The pubovaginal sling procedure is usually performed using general anesthesia. This sling requires an abdominal incision to harvest a rectus fascia graft or leg incisions to harvest a fascia lata graft. This can be done with a scalpel, electrocautery or with the aid of a tissue stripper. Cadaveric slings are not commonly used because of decreased efficacy and lack of durability (resorption and integration risks) and issues with rejection and questions of durability of xenogenic (mostly porcine) tissue slings also limits their use. After a vaginal incision is made, Stamey needles or long clamps are passed from the abdominal incision through the retropubic space. After cystoscopy, the harvested strip of fascia is pulled up transvaginally and the sling is tensioned with a surgical instrument similar to that with a TVT and attached to the rectus fascia with permanent sutures.

While some of plaintiffs' experts claim that another material such as PVDF, Vypro or Ultrapro should be used, they point to no similar breadth and length of clinical data in SUI patients to make such comparisons nor have they provided data showing that these meshes would work long term in the design of the TVT or TVT-O which have long term data. The reason is simple – they cannot. These meshes have not been studied to treat SUI in women like TVT and TVT-O. Their methodology is severely compromised and in effect, unscientific. I know of no pelvic floor surgeons in the state of Texas or in the United States who use PVDF or kits employing PVDF to treat SUI or mixed UI. The same can be said

for Vypro and Ultrapro mesh.

Urology, gynecology and urogynecology specialists and surgeons like me turn to the TVT and TVT-O because it is proven and it works. It is endorsed by urology, gynecology and urogynecology professional societies in the United States, Europe and internationally whereas Plaintiffs' experts' posited alternative mesh design for SUI are not. Also while Vypro, Gynemesh PS and Ultrapro mesh have been suggested as potential better design, I would have concern with a potential decrease of efficacy if utilized as a sling given the mesh in a SUI sling is only about 1 centimeter wide. This narrow strip of tape needs pores like that in the TVT and TVT-O mesh as the mesh provides for a backboard at the midurethra. Vypro and Ultrapro also have a partially absorbable component and the data do not show that these meshes would work in the TVT design as the mesh sticks to the sheath and tears apart upon sheath removal, losing integrity. Moreover, when used in pelvic organ prolapse repair they have not been demonstrated to be more efficacious or safer and have exposure rates of 15% and dyspareunia. (Jacquetin 2004 ICS; Milani 2012)

The pore size for the TVT and TVT-O mesh is macroporous (> 75 microns) and allows the cells needed to address bacteria and promote tissue incorporation. Plaintiffs' experts' claim that 1,000 microns are needed in each direction in order for a mesh to have effective porosity is a theory and artificial construct and the clinical data on the TVT and TVT-O mesh as discussed later is inconsistent with this theory. Moreover, the porosity of the TVT and TVT-O mesh is among the largest for any SUI sling and is optimal for use in the TVT configuration. Lastly, these other meshes can also lead to mesh exposure, which is a wound complication.

There are risks with all surgeries. All SUI surgeries have potential risks. All surgical procedures to treat SUI can fail. All surgical procedures have some degree of pain and discomfort. All surgical procedures to treat SUI may require reoperation for failure or to treat complications. For example, as discussed later in the SISTEr trial that was conducted by the Urinary Incontinence Network, 47% of the Burch patients and 63% of the fascial sling patients had adverse events. (Albo ME, Burch colposuspension versus fascial sling to reduce urinary stress incontinence. N Engl J Med. 2007; 356:2143- 55.)

The risks of SUI surgery include:

Damage to organs like the bladder

Ureteral injury

Damage to bowel

Damage to vessels

Damage to nerves

Anesthesia risks

Wound complications some requiring surgical intervention

Infection

Incisional hernia

Wound dehiscence (wound edge separation)

Seroma or hematoma

Granulation tissue or stitch granulations

Inflammation

Bleeding

Need for blood transfusion

Blood clot

DVT

Fistula

Erosion of suture (ie, into bladder)

Urinary tract infection (recurrent)

Recurrent cystitis (urinary bladder inflammation)

Catheter complications

Voiding dysfunction / difficulty

De novo detrusor overactivity

De novo urgency urinary incontinence

Urinary retention

Urinary frequency

Need for self-catheterization

Persistent Voiding dysfunction

Voiding dysfunction leading to surgical revision

Pain

Pain to the groin

Pelvic pain

Dyspareunia (Pain with sex)

Numbness or weakness from the surgery

Gastrointestinal problems

Bowel adhesion

Development of vaginal wall prolapse

Ileus / bowel obstruction

Abdominal scar after Burch surgery

Need for repeat surgery

Urologists, Ob/Gyns and urogynecologists are trained on the risks of these surgeries in residency and fellowship. SUI surgery, including the TVT and TVT-O, are taught at many residencies and fellowship programs in the United States and Texas specifically. Mesh exposure/erosion is the only unique complication of the TVT and TVT- O as compared to other SUI surgeries. (FDA March 27, 2013 Statement, Considerations about Surgical Mesh for SUI; AUA October 2013 Position Statement on the Use of Vaginal Mesh for the Surgical Treatment of Stress Urinary Incontinence). Moreover, colposuspension and fascial sling procedures rely on the use of permanent sutures, which can also lead to erosion, and wound complications also occur with these procedures. In particular the large abdominal incision is susceptible to wound herniation, seroma and infection and leads to scarring. Pain and nerve injury can also occur with the incision and secondary surgical site harvesting of fascia lata as well. Voiding dysfunction after SUI surgery, and associated with tensioning of sutures and biologic and synthetic slings, can occur with all SUI surgeries. Pain and dyspareunia can occur with all SUI surgeries, as can organ damage and bladder perforation. Knowledge of these risks is a

basic part of female pelvic surgery training and from my standpoint as a medical doctor, these risks do not need to be incorporated into the TVT-O IFU. Surgeons would be aware of these risks from their basic training and experience. Moreover these risks are obvious to pelvic floor surgeons performing SUI surgeries given the described surgical techniques and instruments and materials used during SUI surgery.

The Burch colposuspension procedure and the pubovaginal sling, using autologous rectus fascia, were studied in the SISTEr trial. (Albo ME., N Engl J Med. 2007;356:2143-55.) 520 of 655 women (79%) completed the outcome assessment. At 24 months, cumulative success rates were higher for women who underwent the fascial sling procedure than for those who underwent the Burch procedure, for both the overall category of success (47% vs. 38%, P=0.01) and the category specific to stress incontinence, which included no self-reported symptoms of stress incontinence, a negative stress test, and no retreatment for stress incontinence (66% vs. 49%, P<0.001).

Moreover, as reported in Figure 4, at 2 years the failure rate was 70% with the Burch and 57% for the sling in the overall category, and the failure rate for SUI specific criteria was 59% with the Burch and 40% with the fascial sling. Overall adverse events were higher with the fascial sling procedure (63% vs 49% in the Burch group) and more women in the fascial sling group had urinary tract infections, difficulty voiding, and postoperative urge incontinence. In the extended SISTEr trial, urinary continence rates decreased during a period of 2 to 7 years postoperatively from 42% to 13% in the Burch group and from 52% to 27% in the sling group, respectively. (Richter H, et al. Patient Related Factors Associated with Long-Term Urinary Continence After Burch Colposuspension and Pubovaginal Fascial Sling Surgeries. J Urol.

2012; 188:485-9.) This study shows that rates with both procedures continue to decline over the longer term.

The TVT device was revolutionary in the field of SUI surgery. It was designed and developed by surgeons over many years of study. (Petros P. Creating a gold standard surgical device: scientific discoveries leading to TVT and beyond: Ulf Ulmsten Memorial Lecture 2014. Int Urogynecol J. 2015; 26:471-6.) Testing led to the development of the Integral Theory and numerous meshes such as Mersilene, Gore-Tex, Teflon and Marlex were tried in the device that would become the TVT, but with higher levels of erosion and tape rejection. (Petros PE, Ulmsten UI. An integral theory and its method for the diagnosis and management of female urinary incontinence. Scand J Urol Nephrol Suppl. 1993; 153:1-93; Ulmsten U, et al. An ambulatory surgical procedure under local anesthesia for treatment of female urinary incontinence. Int Urogynecol J Pelvic Floor Dysfunct. 1996; 7:81-5; Falconer C, et al. Influence of different sling materials on connective tissue metabolism in stress urinary incontinent women. Int Urogynecol J Pelvic Floor Dysfunct. 2001; 12 Suppl 2:S19-23.) Mersilene tape was found to induce a significant inflammatory reaction in paraurethral tissues, with a significant increase in collagen solubility by pepsin. (Falconer C, et al. Clinical outcome and changes in connective tissue metabolism after intravaginal slingplasty in stress incontinent women. Int Urogynecol J Pelvic Floor Dysfunct. 1996; 7:133-7.)

By 1996 the macroporous Prolene polypropylene mesh tape was found to be optimal for use in the TVT as a 1cm wide piece of tape covered by a protective sheath, with high efficacy, low morbidity and low rates of mesh exposure. A tissue reaction study in women showed that there was proper tissue integration and minimal inflammatory reaction. (Falconer C, et al. Influence of different

sling materials on connective tissue metabolism in stress urinary incontinent women. Int Urogynecol J Pelvic Floor Dysfunct. 2001; 12 Suppl 2:S19-23.) The authors reported there was practically no tissue reaction at all seen 2 years after TVT surgery when Prolene mesh was used (Fig. 3), no tape rejections, and there was no change in collagen extractability in the Prolene group (Fig. 1). Additionally, there were no histological differences between paraurethral connective tissue in biopsies from patients operated on with Prolene tape and in controls 2 years after surgery. Lastly, there was no statistical difference in collagen concentration or extractability. Conversely, Mersilene showed two rejections, an intense inflammatory response, and a significant increase in collagen extractability by pepsin. By the time that TVT-O was released, the TVT had been successfully utilized in hundreds of thousands of patients, demonstrating high efficacy, a minimally invasive placement and low morbidity and complications. The TVT-O sling uses the same macroporous Prolene polypropylene mesh as the TVT.

Data cited in my report shows the macroporous Prolene polypropylene mesh tape used in the TVT and TVT-O to be universally accepted as the best material and most biocompatible for use in SUI. These include the highest levels of evidence such as Cochrane reviews, SUI Guidelines, systematic reviews and metaanalyses, and RCTs. Cochrane Reviews are systematic reviews of primary research in human health care and health policy, and are internationally recognized as the highest standard in evidence- based health care. They investigate the effects of interventions for prevention, treatment and rehabilitation. (http://community.cochrane.org/cochrane-reviews)

For example the Ford 2015 Cochrane Review included 81 trials that evaluated 12,113 women the majority of which concerned

the TVT and TVT-O devices. (Ford AA, Rogerson L, Cody JD, Ogah J. Mid-urethral sling operations for stress urinary incontinence in women. Cochrane Database Syst Rev. 2015 Jul 1;7:CD006375. PMID: 26130017.) They found that mid urethral slings have been the most extensively researched surgical treatment for SUI in women and have a good safety profile. Irrespective of the routes traversed, they are highly effective in the short and medium term, and accruing evidence demonstrates their effectiveness in the long term. This review illustrates their positive impact on improving the quality of life of women with SUI. With the exception of groin pain which mostly resolved in the first 6 months, fewer adverse events occur with employment of a transobturator approach. The trials showed that over 80% of women with stress urinary incontinence are cured, or have significant improvement in their symptoms, with either operation, for up to five years after surgery. There is moderate quality evidence that overall reported rates of tape-related complications are low, such as erosion of the tape into the vagina at about 2% for both routes of tape insertion. The reported occurrence of problems with sexual intercourse including pain was low, and leakage of urine during intercourse are improved following insertion of these tapes. They also assessed complication rates derived from several registries involving thousands of patients, again the majority of whom received a TVT or TVT-O device, and reported low rates that were consistent with their primary analysis:

Event	**TVT**
Bladder perforation	2.7 - 3.9%
Reoperation rates relating to tape insertion or voiding	1.6 – 2.4%

dysfunction	
Urinary retention	1.6%
Pelvic hematoma	0.7 – 1.9%
Infection rate	0.7%
Vaginal tape erosion / extrusion	1.5%
Groin pain	0.4%

Additionally, Ford reported that type 1 mesh like that in TVT and TVT-O: has the highest biocompatibility with the least propensity for infection. Differences in their efficacy and complications are likely to be due to several factors including the different knits and weaves of the various tape materials, their biomechanical properties and histological biocompatibility. Pore size affects the inflammatory response and resultant connective tissue formation within the mesh structure. : thus macroporous meshes promote tissue host ingrowth with macrophages, leukocytes, fibroblasts, blood vessels and collagen to transverse the > 75 um pores. These factors allow for and result in biocompatibility and low risk of infection (Amid P. Classification of biomaterials and their related complications in abdominal wall hernia surgery. Hernia 1997; 1:15–21). Monofilament tapes are widely available and now predominate in current clinical practice.

As a result, macroporous, monofilament Prolene polypropylene mesh and the TVT and TVT-O have been specifically recommended for SUI treatment in light of the large body of data

supporting the devices. (NICE (National Institute for Health and Care Excellence) Clinical Guideline 171 - Urinary incontinence: The management of urinary incontinence in women, Sept. 2013). The NICE SUI Guideline recommends that when offering a synthetic mid-urethral tape procedure, surgeons should:

- use procedures and devices for which there is current high quality evidence of efficacy and safety [11]
- only use a device that they have been trained to use
- use a device manufactured from type 1 macro porous polypropylene tape

consider using a tape coloured for high visibility, for ease of insertion and revision. Footnote 11 referenced above states that the guideline only recommends the use of tapes with proven efficacy based on robust RCT evidence and identified TVT and TVT-O as meeting these criteria. As noted above, the TVT and TVT-O include a macroporous (large pore > 75 microns), monofilament polypropylene mesh covered with a sheath that is attached to trocars / helical passers. The TVT is inserted via vaginal incision retropubically and the TVT-O is inserted via vaginal incision through the obturator (it is an "inside-out" transobturator passage). The sling is not anchored. Instead, tissue grows into the mesh and the mesh is held in place. The sling works by providing support to the urethra, for example, when a woman coughs, sneezes or exercises. During TVT placement cystoscopy is performed to detect potential bladder perforation, a potential risk that is well known, warned of, and easy to manage intraoperatively. With the TVT-O, which passes through the obturator foramen, a cystoscopy is not needed, but surgeons are always free to

perform one if they choose to do so. While plaintiffs' experts seem to take issue with blind passage of instruments, similar procedures are used during the placement of an autologous sling. Moreover, the Burch colposuspension which is performed in an open manner can lead to bladder and bowel injury. (Schimpf MO, et al. Society of Gynecologic Surgeons Systematic Review Group. Sling surgery for stress urinary incontinence in women: A systematic review and meta-analysis. Am J Obstet Gynecol. 2014; 211:71.e1-71; AUA 2012 update to SUI Guidelines. https://www.auanet.org/common/pdf/education/clinical-guidance/Incontinence.pdf) Overall the rates of serious complications is less with TVT and TVT-O.

The sling is placed in the space between the vaginal wall and the urethra. When placed as described in the standard fashion, it does not traverse near the bladder or urethra. The mesh is taught to be placed tension-free at the midurethra with the aid of a blunt instrument between the urethra and sling, the sheath is removed, the ends are cut, the excess mesh is excised, and the small incisions are closed.

While plaintiffs' experts make claims about particle loss, I have not observed this clinically and even if particles were to get into the vagina, there would be no clinically significant effect. The particles are of the same Prolene polypropylene that make up the mesh. Moreover, Prolene polypropylene has long been used as a suture in various applications for decades, including orthopedics, cardiovascular surgery, general surgery, urology and Gynecology to mention a few. The clinical data on TVT and TVT-O also do not describe particle loss as playing any significant role on efficacy, which is high, or complications, which are low as discussed in my report. Also, during the surgery the site can be irrigated and

suctioned, which would dispose of any particles. Their claims regarding significant stretching of the mesh as seen on a machine in a lab leading to particle loss, mesh roping and curling are also not clinically significant. The mesh is not used in this manner clinically, as the bench testing removes the trocar, which provides a pathway for the mesh to traverse, and also removes the protective sheath. The protective sheath over the mesh bears the forces as the mesh is passed through the pelvis and as noted the mesh is placed tension free and spaced from the urethra with an instrument like a dilator before removing the sheaths. Also, surgeons do not pre-stretch the mesh to 50% elongation before placement of the TVT and TVT-O. Additionally, the mesh can be repositioned or replaced during the procedure. Mesh particles seen in packaging are also of no clinical concern for these reasons.

The Nilsson 17 year study of the TVT mesh demonstrated excellent efficacy over the long term and very low complications. Objective cure, defined as a negative stress test, was seen in 42 out of 46 women (91.3 %). Two of the women with a positive stress test were regarded as failures, while one woman considered herself significantly improved, even though she had minimal leakage at her stress test. 87.2 % regarded themselves cured or significantly better than before surgery and 50 out of 51 (98 %) would recommend the TVT procedure to a friend. The single tape complication seen during this prospective observational trial during a 17-year period was a small symptom-free exposure of the tape in a completely asymptomatic, continent and highly satisfied 69-year-old woman with an atrophic vaginal mucosa. She was prescribed local estrogen therapy. No other adverse effects, signs or reactions of the tape material could be detected among the women examined. These data have been replicated in several other studies assessing the TVT and TVT-O. The Nilsson 17 year study also showed that there

was no shrinkage of the TVT mesh over time, as suggested by PVR volumes within normal ranges, except for 2 patients with concomitant diseases (Parkinson's, grade III cystocele). Similar data are seen in another prospective study where unchanged resting Q-tip angles confirm the tension-free concept of TVT and there was no shrinkage or tightening of the sling. (Lukacz ES, et al. The effects of the tension-free vaginal tape on proximal urethral position: a prospective, longitudinal evaluation. Int Urogynecol J Pelvic Floor Dysfunct. 2003; 14:179-84.) Other sling materials, such as cadaveric fascia, have been associated with significant tissue reaction and have been shown to shrink and or disappear over time (Fokaefs ED, etal. Experimental evaluation of free versus pedicled fascial flaps for sling surgery of urinary stress incontinence. J Urol 1997; 157:1039–1043). The authors noted that the TVT seems to be more elastic and associated with less tissue reaction than other materials. Falconer evaluated the TVT material in postoperative biopsy specimens from women undergoing the procedure and found minimal inflammation without a significant change in collagen solubility or significant foreign-body reaction. (Falconer C, et al. Influence of different sling materials on connective tissue metabolism in stress urinary incontinent women. Int Urogynecol J Pelvic Floor Dysfunct. 2001; 12 Suppl 2:S19-23.) Moreover, the low complication rates seen long term also contradict Plaintiff's experts' claims that the TVT mesh significantly contracts.

It is my opinion that the TVT and TVT-O are the gold standard and current standard of care for the treatment of SUI. It is my opinion that the TVT and TVT-O are safe and effective. My opinions are supported by the major urologic and urogynecologic surgeon associations and societies. (NICE (National Institute for Health and Care Excellence) Clinical Guideline 171 - Urinary incontinence: The management of urinary incontinence in women, Sept. 2013; AUA

Position Statement on the Use of Vaginal Mesh for the Surgical Treatment of Stress Urinary Incontinence, Oct. 2013; AUGS Position Statement on Restriction of Surgical Options for Pelvic Floor Disorders, March 2013; AUGS & SUFU (Society of Urodynamics, Female Pelvic Medicine and Urogenital Reconstruction) Position Statement on Mesh Midurethral Slings for Stress Urinary Incontinence, Jan. 3, 2014; IUGA (International Urogynecological Association) Position Statement on Mid-Urethral Slings for Stress Urinary Incontinence, July 2014; Schimpf MO, et al. Society of Gynecologic Surgeons Systematic Review Group. Sling surgery for stress urinary incontinence in women: A systematic review and meta- analysis. Am J Obstet Gynecol. 2014; 211:71.e1-71.).

The AUA October 2013 Statement, which I agree with, concluded that:

Suburethral synthetic polypropylene mesh sling placement is the most common surgery currently performed for SUI. Extensive data exist to support the use of synthetic polypropylene mesh suburethral slings for the treatment of female SUI, with minimal morbidity compared with alternative surgeries. Advantages include shorter operative time/anesthetic need, reduced surgical pain, reduced hospitalization, and reduced voiding dysfunction. Mesh-related complications can occur following polypropylene sling placement, but the rate of these complications is acceptably low. Furthermore, it is important to recognize that many sling-related complications are not unique to mesh surgeries and are known to occur with non-mesh sling procedures as well. It is the AUA's opinion that any restriction of the use of synthetic polypropylene mesh suburethral slings would be a disservice to women who choose surgical correction of SUI. Additionally, both

the Society of Urodynamics, Female Pelvic Medicine and Urogenital Reconstruction (SUFU) and the AUA support the use of multi-incision monofilament midurethral slings for the treatment of SUI in properly selected patients who are appropriately counseled regarding this this surgical procedure by surgeons who are trained in the placement of such devices, as well as the recognition and management of potential complications associated with their use.

Multiple case series and randomized controlled trials attest to the efficacy of synthetic polypropylene mesh slings at 5-10 years. This efficacy is equivalent or superior to other surgical techniques. There is no significant increase in adverse events observed over this period of followup. Based on these data, the AUA Guideline for the Surgical Management of Stress Urinary Incontinence (2009) concluded that synthetic slings are an appropriate treatment choice for women with stress incontinence, with similar efficacy but less morbidity than conventional nonmesh sling techniques.

The March 2013 AUGS Position Statement similarly concluded based on high level evidence that full-length midurethral slings, both retropubic and transobturator, have been extensively studied, are safe and effective relative to other treatment options and remain the leading treatment option and current gold standard of care for stress incontinence surgery.

In 2014, SUFU which has over 500 members, and AUGS which has over 1,700 members, issued a Position Statement which analyzes high level data including level 1 Cochrane Review, RCTs and long term study of the TVT mesh and discusses the acceptance and utility of the TVT and TVT-O midurethral slings. They observe that “The polypropylene mesh midurethral sling is the recognized worldwide standard of care for the surgical treatment of stress

urinary incontinence. The procedure is safe, effective, and has improved the quality of life for millions of women." I am in agreement with this statement. Numerous data cited in my report show that the macroporous Prolene polypropylene tape is well tolerated and provides lasting efficacy for SUI. For example, in the 10 year study by Svenningsen which evaluated 483 women at a median duration of 129 months follow-up, there was a 90% objective cure rate, only 2.3 % of the women had undergone repeat SUI surgery, and the total number of exposures was 4 (0.8 %) for the whole 10-year period, with only 1 case of asymptomatic mesh exposure (0.2%) found at the 10-year follow-up. (Svenningsen R, et al. Long-term follow-up of the retropubic tension-free vaginal tape procedure. Int Urogynecol J. 2013; 24:1271-78.)

In the 10 year study by Serati, the 10 year subjective, objective, and urodynamic cure rates were 89.7%, 93.1%, and 91.4%, no patient required tape release or section during the 10 year follow-up, and there were no vaginal, bladder, or urethral erosion, or de novo dyspareunia noted. (Serati M, et al. Tension-free vaginal tape for the treatment of urodynamic stress incontinence: efficacy and adverse effects at 10-year follow-up. Eur Urol. 2012; 61:939-46). More recently, the 13 year study results by Serati were published and showed excellent efficacy and safety. (Serati M, et al. TVT for the treatment of urodynamic stress incontinence: Efficacy and adverse effects at 13-year follow-up. Neurourol Urodyn. 2015 Oct 19. doi: 10.1002/nau.22914. [Epub ahead of print]) The 13 year subjective, objective, and urodynamic cure rates were 85.5%, 90.9%, and 89.1%. Additionally, no patient required tape release or section during the 13 year follow-up, and there were no vaginal, bladder, or urethral erosion, or de novo dyspareunia noted. In the 10.5 year study by Heinonen, objective and subjective cure rates were 90% and 78% and only three

patients (2.3%) had adverse events at 1–11 years postoperatively. (Heinonen P, et al. Tension-free vaginal tape procedure without preoperative urodynamic examination: long-term outcome. Int J Urol. 2012; 19:1003-9.) Two patients with retention and pain had the tape cut without any further problems and the other patient had recurrent urinary tract infections and dysuria as a result of tape erosion into the bladder.

In the 10 year study by Aigmueller, only 2.8% of patients (4/141) had repeat incontinence surgery and there were 2 mesh related reoperations (1.4%) due to mesh erosion. (Aigmueller T, et al. Ten-year follow-up after the tension-free vaginal tape procedure. Am J Obstet Gynecol. 2011; 205:496.e1-5.) In the study by Olsson with a median 138 month follow up, there was only one case (0.8%, 1/124) of wound healing which occurred two months post-operatively, three cases of early tape release (2.4%) for retention, and there were no late adverse effect including erosion of tape rejection at long term follow up. (Olsson I, et al. Long-term efficacy of the tension-free vaginal tape procedure for the treatment of urinary incontinence: a retrospective follow-up 11.5 years post-operatively. Int Urogynecol J. 2010; 21:679-83). These data are inconsistent with Plaintiff's experts' theories.

There are no reliable scientific data that not show a risk of cancer and reliance by Plaintiff's experts on MSDS sheets and data in rats while attempting to extrapolate to humans is unreliable and improper methodology. (Moalli P, et al. Polypropylene mesh: evidence for lack of carcinogenicity. Int Urogynecol J. 2014; 25:573-6; King AB, Goldman HB. Current controversies regarding oncologic risk associated with polypropylene midurethral slings. Curr Urol Rep. 2014; 15:453.) There are no epidemiologic data which shows that there is a statistically significant risk compared to the background rate of malignancy. King reported a series of

2,361 polypropylene midurethral slings with a follow-up extending up to 122.3 months and the rate of cancer formation was 0.0 % and no sarcomas were reported. (King AB, et al. Is there an association between polypropylene midurethral slings and malignancy? Urology 2014; 84:789-92). As observed by AUGS and SUFU in their 2014 Frequently Asked Questions by Providers on MUS for SUI:

Tumors related to the implantation of surgical grade polypropylene for mid- urethral slings in humans have never been reported. There is no compelling evidence supporting human malignant transformation related to polypropylene despite the millions of individuals implanted with various forms of this material spanning well over a half century world-wide. The possibility that biomaterial prosthetic devices could cause tumors or promote tumor growth has been the focus of extensive research by both clinicians and biomaterial researchers. (McGregor, D.B., et al., Evaluation of the carcinogenic risks to humans associated with surgical implants and other foreign bodies - a report of an IARC Monographs Programme Meeting. International Agency for Research on Cancer. Eur J Cancer, 2000. 36(3): p. 307-13; Ratner, B.D., et al., eds. Biomaterials Science: An Introduction to Materials in Medicine - 3rd Edition. 2013, Academic Press: Waltham, MA.) It is known that tumor formation related to biomaterials in animals is largely dependent on the physical, not the chemical configuration of the implant, with smooth large surface areas (discs and thin sheets) being potentially carcinogenic, and irregular disrupted surfaces (e.g. those that contain pores as in meshes) lacking carcinogenicity (Ratner, B.D., et al., eds. Biomaterials Science: An Introduction to Materials in Medicine - 3rd Edition. 2013, Academic Press: Waltham, MA.; Oppenheimer, B.S., et al., The latent period in carcinogenesis by plastics in rats and its relation to the

presarcomatous stage. Cancer, 1958. 11(1): p. 204-13.).

Most recently, a study of 2,474 patients who underwent polypropylene sling placement and followed for a median of 5 years demonstrated that there is no association between polypropylene and cancer or sarcoma in humans. (Linder 2016). Only 2 malignancies (0.08 %) occurred after sling placement while there 49 cancer diagnoses which preexisted the sling placement, demonstrating a much higher background rate of cancer. No cases were seen in patients with more than 10 years follow up. No data have shown a statistically significant higher rate of sarcoma formation or cancer compared to background rates in women.

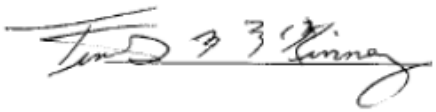
Overall the data show that the TVT and TVT-O are safe and effective. The TVT was developed to provide for a less invasive, less morbid SUI surgery that could be performed in an ambulatory manner. The data show that it is highly effective in the long term and has less complications and in particular serious complications and voiding difficulties than the Burch colposuspension and autologous sling. The TVT-O followed in its design and it demonstrates high levels of efficacy along with an even lower rate of serious complications. Like the TVT, the TVT-O is minimally invasive, less morbid and has less complications than the Burch colposuspension and autologous sling. Overall TVT and TVT-O lead to shorter operating times, shorter hospital stay, reduced operative pain, reduced voiding dysfunction, and a quicker recovery. TVT and TVT-O are the most studied devices for SUI surgery and they have been studied more than the Burch colposuspension and autologous sling. The macroporous Prolene polypropylene tape in TVT and TVT-O is the optimal material for SUI surgery. It is biocompatible and has demonstrated tolerability. Complications are low and manageable. While mesh exposure can occur, other wound complications occur in a significant portion of

patients undergoing the Burch colposuspension and autologous sling. The design of both devices was and is state of the art and the vast majority of pelvic surgeons in the US and abroad prefer the polypropylene midurethral sling over the Burch colposuspension and autologous sling.

Potential risks of SUI surgery are well described to surgeons during training, in medical textbooks, and in the medical literature, and are well known elemental risks that surgeons would be aware of and are in common for most pelvic floor reconstruction. The Bergman study of 1995 demonstrates what we had before TVT/ TVT-o and had serious shortcoming, especially with the standard at that time being the Kelly plication (37% 5 yr success rate) and Needle suspension slings of the Stamey / Raz variety (42%). It was also pointed out by Zivkovic and later by Benson that the dissections around the urethra lead to a 40-65% denervation of the nerves to the sphincter and in doing that lead to Intrinsic Sphincter Deficiency. The minimally invasive Mid Urethral slings have been a tremendous advance and represent an escape from the dark- ages. I believe with all my educational prowess that TVT / TVT-O is the safest and most effective surgery for Stress urinary incontinence with the least risks of complications vs all invasive incontinence surgeries.

All of the opinions I express in this report are held to a reasonable degree of medical and scientific probability and certainty. If I receive additional information after signing this report but before trial, I may form additional or different opinions.

Sincerely,



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